Claims 1-16, 18-19, 23, 29-30, 36-39, and 46-47 are canceled solely in response to the restriction requirement and without prejudice to their presentation in an appropriately-filed divisional application.

Support for the amendments to claims 17, 20, 22, and 34 may be found in the specification at page 7, line 16 to page 8, line 2 and at page 32, line 23 to page 33, line 9.

New claim 52 is supported by page 3, lines 14-17, of the specification.

Support for new claim 53 may be found in the specification at page 3, lines 14-17, page 5, lines 7-12, and page 31, lines 19-21.

Support for new claim 54 may be found in the specification at page 5, lines 13-14.

New claims 55-56 are supported at page 31, lines 16-19 of the present specification.

Support for new claim 57 may be found in the specification at page 11, lines 2-3.

New claim 58 is supported in, for example, the Examples in the specification.

New claims 59-60 are supported in the specification at page 11, lines 5-10.

Support for new claim 61 may be found in the specification at page 4, lines 28-29.

New claim 62 is supported at page 18, lines 22-24 and pages 110-121 of the specification.

The 35 U.S.C. § 101 rejection

The Examiner rejected claim 51 under 35 U.S.C. § 101. The cancellation of claim 51 renders the Examiner's rejection moot. Thus, withdrawal of the rejection of claim 51 under 35 U.S.C. § 101 is respectfully requested.

The 35 U.S.C. § 112, second paragraph, rejections

The Examiner rejected claims 17, 20, 22, 34, 41-44, and 51 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner asserts that the peptide of interest has an arbitrary name. The amendments to the claims, and the cancellation of claim 51, overcome this rejection, and so withdrawal of this rejection is respectfully requested.

The Examiner also rejected claims 17, 20 and 41-44 under 35 U.S.C. § 112, second paragraph, as indefinite for the recitation of the term "indication". This rejection is respectfully traversed.

Applicant discloses that indications of the present invention are those indications associated with chemokine-induced activity, such as aberrant or pathological inflammatory processes (page 18, lines 9-10 and page 98, lines 9-10). Applicant further discloses that indications associated with chemokine-induced activity include: atherosclerosis and other forms of local or systemic vasculitis, diseases such as myocardial infarction, stroke and acute ischemia which are secondary to atherosclerosis; hypertension; reperfusion injury; aortic aneurysms; vein graft hyperplasia; angiogenesis; hypercholesterolemia; congestive heart failure; Kawasaki's disease; stenosis or restenosis, particularly in patients undergoing angioplasty; pathologically low bone mineral density, such as osteoporosis; ulcerative colitis; chronic obstructive pulmonary disease; infection with HIV, other lentiviruses or retroviruses with similar mechanisms of cell entry via chemokine receptor(s), or infection with other viruses, e.g., cytomegalovirus, or viral infection resulting in viral meningitis; organ transplantation, such as acute transplant rejection, allograft rejection and graft versus host disease; transplant vasculopathy; malaria and other consequences of infection by parasites related to plasmodium; asthma; allergic diseases, such as atopy (IgE-mediated components), allergic rhinitis, atopic dermatitis, anaphylaxis, allergic bronchopulmonary aspergillosis (IgE-mediated), and hypersensitivity pneumonitis (high IgG and reactive T cells) (pigeon breeders disease, farmer's lung disease, humidifier lung disease, malt workers' lung disease); allergies, including flea allergy dermatitis in mammals such as domestic animals, e.g., dogs and cats, contact allergens including mosquito bites or other insect sting allergies, poison ivy, poison oak, poison sumac, or other skin allergens; urticaria; eczema; pulmonary fibrosis such as idiopathic pulmonary fibrosis; cystic fibrosis; hemolytic uremic syndrome; autoimmune disorders, including, but not limited to, type I diabetes, Crohn's disease, multiple sclerosis, arthritis, rheumatoid arthritis, systemic lupus erythematosus, autoimmune (Hasimoto's) thyroiditis, autoimmune liver diseases such as hepatitis and primary biliary cirrhosis, hyperthyroidism (Graves' disease; thyrotoxicosis), insulin-resistant diabetes, autoimmune adrenal insufficiency (Addison's disease), autoimmune oophoritis, autoimmune orchitis, autoimmune hemolytic anemia, paroxysmal cold hemoglobinuria, Behcet's disease, autoimmune thrombocytopenia, autoimmune neutropenia, pernicious anemia, pure red cell anemia, autoimmune coagulopathies, myasthenia gravis, autoimmune polyneuritis, experimental allergic encephalomyelitis, pemphigus and other bullous diseases, rheumatic carditis,

Goodpasture's syndrome, postcardiotomy syndrome, Sjogren's syndrome, polymyositis, dermatomyositis, and scleroderma; eye diseases such as uveitis or blinding Herpes stromal keratitis; liver disease; erhlichiosis or Lyme disease including Lyme arthritis; aberrant hematopoiesis; nephritis due to, for example, autosomal dominant polycystic kidney disease, diabetic nephropathy, IgA nephropathy, interstitial fibrosis, or lupus; as well as other disease states resulting from inappropriate inflammation, either local or systemic, for example, irritable or inflammatory bowel syndrome, psoriasis, delayed type hypersensitivity, Alzheimer's disease, chronic pulmonary inflammation, e.g., pulmonary alveolitis and pulmonary granuloma, gingival inflammation or other periodontal disease, and osseous inflammation associated with lesions of endodontic origin, hypersensitivity lung diseases such as hypersensitivity pneumonitis, and inflammation related to histamine release from basophils, such as hay fever, histamine release from mast cells, or mast cell tumors, types of type 1 hypersensitivity reactions (anaphylaxis, skin allergy, hives, allergic rhinitis, and allergic gastroenteritis); glomerulonephritis; inflammation associated with peritoneal dialysis; pancreatitis; neoplasia, e.g., histocytoma, glioma, sarcoma, osteosarcoma, osteoma, melanoma, Kaposi's sarcoma, small cell lung cancer, and ovarian carcinoma as well as myelosuppression and mucositis associated with chemotherapy; brain or spinal cord trauma, such as after disc surgery; gout; lung disease, e.g., due to respiratory syncytial virus infection of humans, cattle, pigs and the like, or lung injury; strokes; Loeffler's syndrome; chronic eosinophilic pneumonia; pulmonary fibrosis; wound healing; bacterial infection, e.g., bacterial peritonitis or meningitis; granulomatous diseases such as Mycobacteriosis, Pneumocystosis, Histoplasmosis, Blastomycosis, Coccidiomycosis, Cryptococcosis, Aspergillosis, granulomatous enteritis, Candidiasis, foreign body granulomas and peritonitis, pulmonary granulomatosis, Wegener's granulomatosis, leprosy, syphilis, cat-scratch disease, schistosomiasis, silicosis, sarcoidosis and berylliosis; lethal endotoxemia; and indications associated with a weak inflammatory response, e.g., which occur in parasitic infection, e.g., *Leishmaniasis*, trypanosome, *Mycobacterium leprae* or *Mycobacterium tuberculosis* infection, helminth infections, such as nematodes (round worms); (Trichuriasis, Enterobiasis, Ascariasis, Hookworm, Strongyloidiasis, Trichinosis, filariasis); trematodes (fluxes) (Schistosomiasis, Clonorchiasis), cestode (tape worms) (Echinococcosis, Taeniasis saginata, Cysticercosis); visceral works, visceral larva migrans (e.g., *Toxocara*), eosinophilic

gastroenteritis (e.g., *Anisaki* spp., *Phocanema* ssp.), cutaneous larva migrans (*Ancylostoma braziliense, Ancylostoma caninum*), or fungal infection; acute respiratory distress syndrome, relapsing Beheers colitis; asthma; rheumatoid arthritis; endotoxemia; endotoxic shock; Crohn's disease; fever, and flu-like symptoms; acute interstitial pneumonitis; septic and nonseptic shock; acute respiratory distress syndrome; thromboembolic conditions; bone resorption; arthritis; acute graft versus host disease; cerebral malaria; cachexia of tuberculosis or cancer; lung injury; and idiopathic fibrosis (page 47, line 1 to page 50, line 14; see also page 98, line 5 to page 110, line 3).

Thus, one of ordinary skill in the art in possession of Applicant's specification would readily understand the metes and bounds of the term "indication".

It is respectfully submitted that the pending claims are in conformance with the requirements of 35 U.S.C. § 112, second paragraph. Therefore, withdrawal of the § 112(2) rejection of claims 17, 20 and 41-44 is respectfully requested.

The 35 U.S.C. § 112, first paragraph, rejection

The Examiner rejected claims 1-17, 20, 22, 34, 41-44, and 51 under 35 U.S.C. § 112, first paragraph. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

In particular, the Examiner asserts that the specification fails to enable a method of preventing or inhibiting an indication associated with a chemokine-induced activity which comprises the administration of a chemokine peptide 3, a variant or derivative thereof, other than those set forth in SEQ ID numbers 1, 7, 38, 40-44, 65-68, and 72-74 as there is insufficient guidance in the specification as to what constitutes a chemokine peptide 3, a variant or a derivative thereof, and so undue experimentation would be required for one of ordinary skill in the art to make and use Applicant's claimed invention.

As amended, the claims are directed to a method of preventing or inhibiting an indication associated with a chemokine-induced activity which employs an effective amount of a peptide of a chemokine, a variant thereof, a derivative thereof, or combination thereof, wherein the peptide comprises no more than 30 amino acid residues, wherein at least three contiguous residues of the peptide correspond to residues in the carboxyl-terminal half of the mature form of the

chemokine, wherein the three contiguous residues correspond to residues Trp-Val-Gln or Lys-Gln-Lys in human MCP-1, and wherein the peptide inhibits the response induced by the corresponding native chemokine, wherein the chemokine is not interleukin 8 (IL-8) or neutrophil activating protein-2 (NAP-2); a method of preventing or inhibiting an indication associated with hematopoeitic cell recruitment which employs an effective amount of a peptide of a chemokine, a variant thereof, a derivative thereof, or combination thereof, wherein the peptide comprises no more than 30 amino acid residues, wherein at least three contiguous residues of the peptide correspond to residues in the carboxyl-terminal half of the mature form of the chemokine, wherein the three contiguous residues correspond to residues Trp-Val-Gln or Lys-Gln-Lys in human MCP-1, and wherein the peptide inhibits the response induced by the corresponding native chemokine; a method to modulate the chemokine-induced activity of hematopoietic cells at a preselected physiological site which employs an effective amount of a peptide of a chemokine, a variant thereof, a derivative thereof, or combination thereof, wherein the peptide comprises no more than 30 amino acid residues, wherein at least three contiguous residues of the peptide correspond to residues in the carboxyl-terminal half of the mature form of the chemokine, wherein the three contiguous residues correspond to residues Trp-Val-Gln or Lys-Gln-Lys in human MCP-1, and wherein the peptide inhibits the response induced by the corresponding native chemokine; and a method to alter hematopoietic cell-associated activity at a tumor site which employs an effective amount of a peptide of a chemokine, a variant thereof, a derivative thereof, or combination thereof, wherein the peptide comprises no more than 30 amino acid residues, wherein at least three contiguous residues of the peptide correspond to residues in the carboxyl-terminal half of the mature form of the chemokine, and wherein the three contiguous residues correspond to residues Trp-Val-Gln or Lys-Gln-Lys in human MCP-1.

As evidence that Applicant's disclosure would enable the art worker to identify chemokine peptides, variants or derivatives thereof, falling within the scope of the claims, the Examiner is respectfully requested to consider Applicant's detailed specification.

It is disclosed that a peptide of the invention, i.e., an isolated and purified peptide of a chemokine, a variant, or a derivative thereof, may comprise as few as three contiguous residues, and no more than 30 amino acid residues, which correspond to chemokine sequences generally located in the carboxyl-terminal half of the chemokine (see page 7, line 16 to page 8, line 2, page

31, line 25 to page 32, line 11 and Example 7).

For example, Table 1 illustrates an alignment of selected chemokines and indicates the general location of a peptide of the invention in human MCP-1, murine MCP-1, human MCP-2, human MCP-3, human MIP-1α, human MCP-1β, RANTES, eotaxin, IL8 and human SDF-1b. Exemplary chemokines, from which the peptides of the invention may be obtained or derived, are listed at page 31, lines 4-24 of the specification, and include MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIG, MIP1α, MIP1β, MIP2, RANTES, PF-4, I-309, HCC-1, eotaxin, C10, CCR-2, ENA-78, GROα, GROβ, GROγ, IL-8, IP-10, SDF1, SDF1α, SDF1β, MIP3α, TCA-3, CTAPIII, MARC/FYK, β- thromboglobulin, GCP-2, PBP, HC14, MDC, TECK, PARC, 6Ckine, fractaline, DC-CK1, LIX, TARC, LARC, Ckβ8, CCF18/MRP-2, CCIII, CKα2, H1305, Dvic-1, MGSA, Ckβ4, DGWCC, TCA4, dendrokine, CC2/HCC1, CC3, and MIP1τ, vMIP-I, vMIP-II and vMIP-III, NAP-2, γIP, ENA78, lymphotactin, neurotactin and CCIII. Moreover, Applicant provides exemplary examples of chemokine peptide 3 in Figure 14.

It is further disclosed that a peptide of the invention may have 100% contiguous amino acid sequence homology or identity to the amino acid sequence of a native chemokine, or have less than 100% homology to the corresponding amino acid sequence of a nature chemokine, i.e., the peptide is a "variant" peptide. A variant peptide is disclosed as a peptide which has amino acid residues not present in the corresponding wild-type chemokine, e.g., amino acid substitution(s), internal deletion(s) or D-amino acid(s). Chemokine peptides or peptide variants which are subjected to chemical modifications, such as esterification, amidation, reduction, protection and the like, are referred to as chemokine "derivatives." For example, a modification known to improve the stability and bioavailability of peptides *in vivo* is the cyclization of the peptide. Thus, a derivative of a peptide of the invention may include a cyclic reverse sequence derivative (CRD), linear reverse D derivative (LRD) and cyclized forward L derivative (CFL) of a peptide of the invention.

Moreover, the specification provides exemplary *in vitro* and *in vivo* assays to identify whether a chemokine peptide, a variant thereof, or a derivative thereof, inhibits or reduces a chemokine-induced activity (page 50, lines 16-25). These assays include *in vitro* assays (see page 50, line 27-page 52, line 28) which detect whether an agent inhibits the chemokine-induced chemotaxis of a variety of cell types (e.g., neutrophils, monocytes, eosinophils, mast cells,

platelets or lymphocytes; page 52, lines 1-2), inhibits the release of enzymes from certain cells (such as N-acetyl-β-D-glucosamidase from monocytes or elastase from neutrophils; page 53, lines 2-13), changes the concentration of cytosolic free Ca^{2+} in various cell types (monocytes, eosinophils, neutrophils; page 53, line 15-page 54, line 18), inhibits binding to a chemokine receptor and/or displaces bound chemokine (page 54, line 20-page 55, line 27), and inhibits the co-mitogenic activity of a chemokine (page 56, lines 14-20).

Example 1 discloses the use of an *in vitro* chemotaxis assay, i.e., the inhibition of chemokine-induced THP-1 (a monocytic cell line) migration, to identify regions of human MCP-1 (hMCP1) falling within the scope of the invention. Example 4 describes that a CRD peptide variant of MCP-1 inhibited MCP-1-induced THP-1 migration. Table 2 shows the inhibition by a MCP-1 chemokine peptide of the MCP-1-, MIP1α-, IL8- and SDF-1α-induced migration of THP-1 cells and primary human monocytes. Table 4 shows ED_{50} data for four chemokines (MCP-1, MIP1α, IL8 and SDF-1α) and selected peptides which include variants of MCP-1 chemokine peptide, e.g., one variant peptide of human MCP-1 chemokine peptide (the variant is designated $Leu_4Ser_7Ile_{11}$peptide3(1-12)[MCP-1]) has amino acid substitutions at positions 4, 7 and 11 relative to the sequence of a 12 amino acid peptide of human MCP-1 designated peptide 3(1-12)[MCP-1], and another variant (referred to as $Ser_7Glu_8Glu_9$peptide3(1-12)[MCP-1]) has substitutions at positions 7, 8 and 9 relative to peptide 3(1-12)[MCP-1].

Table 4 also includes data from three chemokine peptides having three amino acid residues, one of which is a tripeptide from MIP-1α. Some of the peptides described in Table 4 were found to be pan-chemokine inhibitors, while others showed selectivity for certain groups of chemokines, i.e., selectivity for CC or CXC chemokines. Example 6 discloses additional experiments for tripeptides of the invention. Thus, the tripeptide WVQ, a sequence found in the carboxy-terminal half of MCP-1, MCP-3, MIP-1α, MIP-1β, RANTES, eotaxin and IL8, inhibited all four chemokines tested, while tripeptide KQK, another sequence found in the carboxy-terminal half of MCP-1, was specific for MCP-1 (versus MIP-1α, IL8 or SDF-1α). It is disclosed that the corresponding tripeptides for MIP-1α (SEE), SDF-1 (KLK), and IL8 (KEN) were each specific for the cognate chemokine.

It is further disclosed that the efficacy of a peptide of the invention in an animal model may be assessed by clinical parameters specific for the particular model or by general parameters

such as the extent of inflammation or cellular infiltration into affected tissues (page 66, lines 15-16). Animal models which may be employed to determine whether a peptide of the invention inhibits chemokine-induced activity *in vivo* are exemplified at pages 65-69 of the specification. For example, atherosclerosis is associated with chemokine-induced, e.g., MCP-1-induced, macrophage recruitment. Animal models of atherosclerosis include apoE knockout mice, mice which over express human apoB, and Watanabe heritable hyperlipidemic rabbits (page 66, lines 2-6). Animal models for autoimmune disease include collagen-induced arthritis in DBA/1 mice and myelin basic protein-induced experimental autoimmune encephalomyelitis. Animals models for osteoporosis include ovariectomized female rats, mice and monkeys, rats treated with heparin or glucocorticoids, and suspension-induced osteoporosis in rats. Thus, for atherosclerosis, the extent of lipid lesion formation in vessel walls may be determined in animals that have been administered a peptide of the invention relative to control animals (page 66, lines 24-29). For osteoporosis, bone density may be determined (page 100), as well as the presence bone matrix degradation products in plasma and urine (page 100), in animals that have been administered a peptide of the invention relative to control animals.

Thus, Applicant has provided a disclosure sufficient to enable the art worker to identify agents, i.e., a chemokine peptide 3, a variant thereof, or a derivative thereof, falling within the scope of the claims.

With respect to the "undue experimentation" alleged by the Examiner to be necessary to identify a chemokine peptide, a variant thereof, or a derivative thereof, falling within the scope of the claims other than those exemplified in the present specification, the fact that the outcome of such a synthesis/screening program is unpredictable is precisely why a screening program is carried out. The Examiner simply cannot reasonably contend that a screening program to locate biomolecules with target biological or physical properties would not be carried out by the art because the results cannot be predicted in advance.

In fact, the Federal Circuit has explicitly recognized that the need, and methodologies required, to carry out extensive synthesis and screening programs to locate bioactive molecules do not constitute undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1406-1407 (Fed. Cir. 1988), the Court stated:

The nature of monoclonal antibody technology is that it involves screening

> hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody.

Likewise, practitioners in the art related to the present application would be well-equipped to prepare and screen peptides of chemokines, substituted peptides of chemokines and derivatives thereof to locate additional peptides falling within the scope of the claims. See also, Hybritech Inc. v. Monoclonal Antibodies Inc., 231 U.S.P.Q. 81, 84 (Fed. Cir. 1986) (evidence that screening methods used to identify characteristics [of monoclonal antibodies] were available to art convincing of enablement). Thus, the fact that a given claim may encompass a large number of peptides is not dispositive of the enablement issue, particularly in an art area in which the level of skill is very high and in which the screening of large numbers of compounds has been standard practice for at least ten years (Ex parte Forman, 230 U.S.P.Q.2d 456 (Bd. App. 1986).

It is respectfully submitted that the pending claims are in conformance with the requirements of 35 U.S.C. § 112, first paragraph. Therefore, withdrawal of the § 112(1) rejection of the claims is respectfully requested.

The 35 U.S.C. § 102(a) rejection

The Examiner rejected claims 17, 20, 22, 34, and 51 under 35 U.S.C. § 102(a) as being anticipated by Gong et al. (J. Exp. Med., 186, 131 (1997), "Gong et al. I"). This rejection, as it may be maintained to the pending claims, is respectfully traversed.

Gong et al. I assessed the activity of chemically synthesized human MCP-1 which consists of residues 1-76 of the mature protein ("MCP-1(1-76)"), an antagonist of human MCP-1 which consists of residues 9-76 of mature MCP-1 ("MCP-1(9-76)"), and a control peptide, MCP-1Ala (which has each of the four cysteine residues of MCP-1 replaced with an alanine), in the MRL-*lpr* model of chronic arthritis (abstract). In the model, arthritis is induced in by the administration of complete Freund's adjuvant (CFA) supplemented with *Mycobacterium tuberculosis* H37 RA (page 131). Gong et al. I report that after the mice were primed with CFA, daily injections of the antagonist MCP-1(9-76), i.e., a peptide of 68 amino acid residues in length, prevented the onset of symptoms of arthritis as measured by joint swelling (ankle width) and histopathological evaluation of the joints (Figures 1-3). When MCP-1(9-76) was

administered after disease development, a reduction of the symptoms and histopathology of chronic arthritis was observed, although the authors note that there was a variation in the magnitude of response among individuals (abstract, page 134, second column and Figures 5-6). In contrast, the administration of MCP-1(1-76) and the control peptide MCP-1Ala following CFA injection did not prevent disease onset or reduce symptoms, in fact, MCP-1(1-76) administration resulted in the earlier onset and a higher incidence of the disease (Figures 1a, 3-4, and 6). The authors note that RANTES(9-68) also inhibits the onset of arthritis in the MRL-*lpr* model (page 135, second column). Gong et al. I do not disclose the use of a chemokine peptide of less than 30 amino acid residues, much less a variant thereof or a derivative thereof.

The Examiner, referring to "Sequence Comparison A", asserts that Gong et al. I teach polypeptides which comprise the peptides of the present application. The comparison shows 100% sequence identity between 10 amino acids of MCP-1 and the query sequence. However, Gong et al. I do not refer to this 10 amino acid sequence, or suggest the use of a chemokine peptide, a variant or a derivative thereof, which comprises 30 amino acid residues or less. Thus, Gong et al. I do not anticipate Applicant's invention.

Therefore, the Examiner is respectfully requested to withdraw the 35 U.S.C. § 102(a) rejection of the claims.

The 35 U.S.C. § 103(a) rejections

The Examiner rejected claims 17, 20, 22, 34, and 51 under 35 U.S.C. § 103(a) as being unpatentable over Gong et al. (J. Exp. Med., 181, 631 (1995), "Gong et al. II"). The Examiner also rejected claims 17 and 41-44 under 35 U.S.C. § 103(a) as being unpatentable over Gong et al. II in view of Sozzani et al. (The Journal of Immunology, 157, 4664 (1996)). As these rejections may be maintained to the pending claims, they are respectfully traversed.

To determine the role of the amino terminal region of MCP-1 in structure and function, Gong et al. II prepared MCP-1 mutant peptides (see Figure 2) which included deletion mutants containing amino acid residues 2-76, 3-76, 4-76, 5-76, 6-76, 7-76, 8-76, 9-76, 10-76 and 11-76 of MCP-1. Gong et al. II relate that some of the mutant MCP-1 peptides, such as those having residues 8-76, 9-76 and 10-76, have receptor antagonist properties (see Figures 8-9 and page 637, second column). Based on the data, the authors predict that the MCP-1(9-76) antagonist will be

in the therapeutic range of effectiveness (page 638, second column).

Despite the Examiner's reference to the 10 amino acid identity in "Sequence Comparison A", Gong et al. II do not disclose or suggest the use of a chemokine peptide of less than 30 amino acid residues, much less a variant thereof or a derivative thereof.

Sozzani et al. relate that 5-oxo-6,8,11,14-eicosatetraenoic acid (ETE) and 5-oxo-15(OH)ETE, collectively referred to as 5-oxo-ETEs, induced directional migration of human monocytes *in vitro*, and, in a synergistic fashion, increased monocyte migration in response to MCP-1, as well as increased MCP-1-induced arachidonic acid release by monocytes (abstract, Figures 6 and 8). Sozzani et al. do not teach or suggest the use of a peptide of a chemokine, a variant thereof, or a derivative thereof, e.g., a chemokine peptide which is no more than 30 amino acid residues in length, e.g.,to inhibit the response induced by the corresponding native chemokine. Hence, Sozzani et al. do not teach or suggest Applicant's invention.

With respect to the rejection of claims 17, 20, 22, 34, and 51 over Gong et al. II, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer to a mammal peptides that correspond to regions of the amino-terminal truncated peptides taught by Gong et al. II to inhibit a chemokine-induced activity. The motivation to do so, according to the Examiner, is found at page 638 of Gong et al. II, which indicates that MCP-1(9-76) will be in the therapeutic range of effectiveness, and will be useful for the development of further MCP-1 receptor antagonists with high potency. The Examiner also asserts that Gong et al. II, which discloses that MCP-1 antibodies inhibit *in vivo* function, provides a reasonable expectation that the administration of chemokine peptides will be efficacious.

With respect to the rejection of claims 17 and 41-44 over the combination of Gong et al. II and Sozzani et al., the Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the amino-terminal truncated peptides of Gong et al. II as inhibitors of arachidonic acid production, and that the motivation to do so is found at page 4670 of Sozzani et al., where Sozzani et al. remark that the metabolism of arachidonic acid is implicated in monocyte chemotaxis.

However, to render a claimed invention obvious, there must be some suggestion or

motivation, either in the cited reference itself or in the knowledge generally available to an art worker, to modify the cited reference or to combine reference teachings so as to arrive at the claimed invention. Moreover, there must be a reasonable expectation of success, i.e., that the invention would be operable. Finally, the prior art reference must teach or suggest all the claim limitations (M.P.E.P. § 2143). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure (M.P.E.P. citing with favor, In re Vaeck, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

There is nothing in Gong et al. II to suggest that chemokine peptides of less than 30 amino acid residues in length would be useful, e.g., to inhibit or prevent a chemokine-induced activity. Moreover, based on the fact that peptides having fewer residues than MCP-1(9-76) were less effective than MCP-1(9-76) (see page 637 of Gong et al. II), one of ordinary skill in the art would not be motivated to generate peptides of MCP-1 that are smaller than 30 amino acid residues in length. And although Gong et al. II mention that anti-MCP-1 antibodies have been reported to, among other things, reduce pulmonary monocyte/macrophage recruitment in a monocyte/macrophage-dependent IgA immune complex alveolitis in the rat, Gong et al. II provide no reason to expect that chemokine peptides of 30 amino acid residues or less, variants thereof, or derivatives thereof, would be effective to alter a chemokine-induced or associated activity. Therefore, Gong et al. II do not render Applicant's invention obvious.

Nor does Sozzani et al. remedy the deficiencies of Gong et al. II. Sozzani et al. relate that agents, i.e., 5-oxo-ETEs, have a synergistic effect with MCP-1, resulting in an increase of arachidonic acid from human monocytes, and an increase in monocyte migration. There is nothing in Sozzani et al. that teaches or suggests the use of a peptide of a chemokine that inhibits the response induced by MCP-1. Thus, Sozzani et al. does not provide the artisan with the motivation to employ chemokine peptides, variants thereof, or derivatives thereof to inhibit a chemokine-induced response. Hence, the combination of Gong et al. II and Sozzani et al. does not render Applicant's invention obvious.

The successful identification of a chemokine peptide of no more than 30 amino acid residues in length, a variant thereof, or a derivative thereof is only provided in Applicant's disclosure, not by the limited and specific disclosures of the cited art. It is well-settled law that it is improper to use Applicant's disclosure to support an obviousness rejection. In re Carroll, 202

U.S.P.Q. 571 (C.C.P.A. 1979); In re Ruff, 256 F.2d 590, 118 U.S.P.Q. 340 (C.C.P.A. 1958). Thus, neither Gong et al. II nor the combination of Gong et al. II and Sozzani et al. render Applicant's invention obvious.

Hence, withdrawal of the rejection of the claims under § 103(a) is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to telephone Applicant's attorney (612-373-6959) to facilitate prosecution of this application. If necessary, please charge any additional fees deemed necessary to Deposit Account 19-0743.

Respectfully submitted,

DAVID J. GRAINGER ET AL.,

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6959

Date August 23, 2000 By [signature]
Janet E. Embretson
Reg. No. 39,665

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner of Patents, Washington, D.C. 20231 on **August 23, 2000**.

Frances Essien
Name

Frances Essien
Signature